

**Evaluation of isolated mild chronic elevation of serum aminotransferases\***

<b>Step 1: Initial evaluation</b>
Review possible links to medications, herbal therapies, or recreational drugs
Screen for alcohol abuse (history, screening instruments, AST/ALT ratio >2:1)
Obtain serology for hepatitis B and C (HBsAg, anti-HBs, anti-HBc, anti-HCV)
Screen for hemochromatosis (Fe/TIBC >45 percent)
Evaluate for fatty liver (AST/ALT usually <1, obtain RUQ ultrasonography)
<b>Step 2: Second-line evaluation (if initial evaluation is unrevealing)</b>
Consider autoimmune hepatitis, particularly in women and in those with a history of other autoimmune disorders (check serum protein electrophoresis; obtain ANA and ASMA if positive)
Obtain thyroid function tests (TSH if hypothyroidism is suspected; otherwise, obtain serum TSH, free T4, and T3 concentrations)
Consider celiac disease (especially in patients with a history of diarrhea or unexplained iron deficiency: serum IgA anti-tissue transglutaminase antibodies)
<b>Step 3: Evaluation for uncommon causes (if second-line evaluation is unrevealing)</b>
Consider Wilson disease, especially in those <40 years of age (check serum ceruloplasmin, evaluate for Kayser-Fleischer rings)
Consider alpha-1 antitrypsin deficiency, especially in patients with a history of emphysema out of proportion to their age or smoking history (obtain alpha-1 antitrypsin level)
Consider adrenal insufficiency (8 am serum cortisol and plasma ACTH, high-dose ACTH stimulation test)
Exclude muscle disorders (obtain creatine kinase or aldolase)
<b>Step 4: Obtain a liver biopsy or observe (if no source identified after steps 1 to 3)</b>
Observe if ALT and AST are less than twofold elevated
Otherwise, consider a liver biopsy

AST: aspartate aminotransferase; ALT: alanine aminotransferase; HBsAg: hepatitis B surface antigen; anti-HBs: antibody to hepatitis B surface antigen; anti-HBc: antibody to hepatitis B core antigen; anti-HCV: antibody to hepatitis C virus; Fe: iron; TIBC: total iron binding capacity; RUQ: right upper quadrant; ANA: antinuclear antibodies; ASMA: anti-smooth muscle antibodies; TSH: thyroid-stimulating hormone; IgA: immunoglobulin A; ACTH: corticotropin.

\* Mild is defined as between 2 and 10 times the upper limit of normal; chronic is defined as more than six months.

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